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A Hebbian Learning Approach for Diffusion Tensor Analysis & Tractography

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1. Introduction

The principle significance of an artificial neural network is that it learns and improves through that learning. The definition of the learning process in neural networks is of great importance. The neural network is stimulated and regarding to these stimulations the free parameters of the network change in its internal structure. As a result the neural network replies in a new way. Based on a basic learning algorithm namely Hebbian learning, a solution to the problem of resolving uncertainty areas in diffusion tensor magnetic resonance image (DTMRI) analysis is represented. Diffusion tensor imaging (DTI) is a developing and promising medical imaging modality allowing the determination of in-vivo tissue properties noninvasively upon the random movement of the water molecules. The method is unique in its ability being a noninvasive modality which is a great opportunity to explore various white matter pathologies and healthy brain mapping for neuroanatomy research. In neuroscience applications DTI is mostly used addressing brain's fiber tractography, reconstructing the connectivity map. Clinical evaluation of fiber tracking results is a major problem in the field. Noise, partial volume effects, inefficiency of numerical implementations by reconstructing the intersecting tracts are some of the reasons for the need of standardized fiber tract atlas. Also misregistration caused by eddy currents, ghosting due to motion artifacts, and signal loss due to susceptibility variations may all affect the calculated tractography results.
The proposed method based on the Hebbian learning provides an instance of non-supervised and competitive learning in a neurobiological aspect as a solution to the tracking problem of the intersecting axonal structures. The main contribution of the study is to describe a tracking approach via a special class of artificial neural networks namely the Hebbian learning with improved reliability.

2. Diffusion tensor imaging

Essential concepts necessary to understand DTMRI are explained in this section. The utility of the diffusion tensor is that it provides the direction in three dimensional space in which

the rate of diffusion is greatest (Basser et al., 2000). The developing imaging modality is almost a routine MR technique analyzing tissue anisotropy characteristics, connectivity and alterations of human brain neural tracts.

The discrete diffusion tensor and diffusivity trajectory estimation between neighboring image pixels are used to trace out the fiber pathways namely the tracts. The process of determining the neural tracts especially white matter structures by diffusion tensor analysis is commonly known as *tractography*. Fiber tractography is able to provide both quantitative and qualitative information aiming to clarify the anatomical architecture of brain's fibers and advance our knowledge of fiber connectivity maps (Ding et al., 2003). There are some limiting cases in DTI analysis and fiber tracking. One of the critical problems in estimating these brain maps is the existence of intersecting tracts within the tissue. As a consequence of this fact, axonal structures in the image voxels with more than one diffusivity direction can not be clearly defined, where the generally the diffusion tensor model becomes inaccurate to define the uncertainties (Bammer, 2003; Ciccarelli et al., 2003).

Current researchs are involved in multi-tensor mixture models (Tuch et al., 2002) and higher order tensor models (Basser et al., 1994; Basser, 2002). Some techniques such as q-space imaging (Callaghan et al. 1988; Basser, 2002), and high angular resolution diffusion imaging (Frank, 2002; Tuch et al., 2002) are enhanced in resolving such multidiffusivities within a voxel. Jones employed the so called "cone of uncertainty" as a construction method where the tensor's principal eigenvector has a confidence interval in which one helps to define the uncertainty regions as a cone with a probability distribution instead of a discrete diffusivity determination (Jones, 2003). In spite of having some proposed methods for determination of the intersecting diffusivities (Westin et al., 1999; Pajevic & Pierpaoli, 2000; Poupon et al., 2000; Tuch et al., 2002), still the connection is not precisely defined, and there isn't any gold standard yet (Westin et al., 1999; LeBihan et al., 2006). So depending on the proposed Hebbian learning rule approach, we aim to clarify the tracts in the intersections in order to eliminate the uncertainty.

3.1 Diffusion tensor theory

Diffusion weighted images are the raw data source for the calculation of the diffusion tensor measured using the Stejskal-Tanner equation (Basser & LeBihan, 1992; Basser et al., 1994), where $|g|$ is the strength of the diffusion gradient pulses, S_0 is the RF signal received for a measurement without diffusion gradient pulses, and S_i is the signal received with diffusion gradient pulses. The *diffusion tensor* $\boldsymbol{D}$ is gained by systematically application of the diffusion weighted gradients in multiple directions. The mathematical expression D is a real, symmetric second order tensor, represented in matrix form as a real, symmetric 3x3 matrix (Eq. 1).

$$S_i = S_0 e^{-b\hat{g}_i^T D \hat{g}_i} \tag{1}$$

Getting the six unique elements of the diffusion tensor D requires at least six diffusion weighted measurements in non-collinear measurement directions g along with a non-diffusion-weighted measurement S_0 based on the three-dimensional Gaussian Stejskal-

Tanner model (Eq.2). The linear system of $n \geq 6$ diffusion weighted measurements constraining the diffusion tensor D may be represented in matrix form (Basser, 2002).

$$\begin{bmatrix} x_1^2 & y_1^2 & z_1^2 & 2x_1y_1 & 2y_1z_1 & 2x_1z_1 \\ x_2^2 & y_2^2 & z_2^2 & 2x_1y_1 & 2y_2z_2 & 2x_2z_2 \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ x_n^2 & y_n^2 & z_n^2 & 2x_ny_n & 2y_nz_n & 2x_nz_n \end{bmatrix} \begin{bmatrix} D_{xx} \\ D_{yy} \\ D_{zz} \\ D_{xy} \\ D_{xz} \\ D_{yz} \end{bmatrix} = \begin{bmatrix} -\frac{1}{b}\ln\frac{S_1}{S_0} \\ -\frac{1}{b}\ln\frac{S_2}{S_0} \\ \vdots \\ -\frac{1}{b}\ln\frac{S_n}{S_0} \end{bmatrix} \tag{2}$$

In the linear system of equations $Ad = s$ of equation 2, A is the encoding matrix containing the $n \geq 6$ unit normalized gradient measurement directions, d is a vector specifying the 6 unique elements of the diffusion tensor D (Eq.3), and s is a vector containing natural logarithmic scaled RF signal loss resulting from the Brownian motion of spins (Berg, 1983).

$$D = \begin{bmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{bmatrix} \tag{3}$$

Diagonalization of the diffusion tensor yields its eigensystem with its eigenvectors and eigenvalues λ_1, λ_2, λ_3 listed in decreasing order. The eigensystem of D is calculated in every pixel for DT analysis. Different research groups have studied mathematical explanations of the diffusion tensor (Lori et al., 2002; Ciccarelli et al., 2003; Khader & Narayana, 2003). The scalar diffusion tensor eigenvalues and their derivatives defining the anisotropy values are correlated to the underlying tissue in the region of interest (ROI). The directional eigenvectors are relevant to the anisotropy spatially and orientationally (Pierpaoli et al., 2002). The largest eigenvector actually corresponds to the major molecular motion of water indicating the principal orientation of the analyzed axonal structures. Most of the diffusion tensor analyses rely in assigning the major eigenvector as the direction of the largest water diffusion called the principal diffusivity for reconstructing the 3D trajectories of human brain fiber bundles (Westin et al., 1999; Basser et al., 2000; Poupon et al., 2000; Khader et al., 2003; Taylor et al., 2004). The approach is adopted in our implementation too. Using the computational diagonalization the eigensystem of the 3 by 3 symmetric D is achieved (Borisenko & Tarapov, 1979; Szafer et al., 1995; Göksel & Özkan, 2006). The eigenvectors e_i and the corresponding eigenvalues λ_i are the solutions of the equation (5), where the eigenvectors e_i (Eq. 4) are the principal diffusion directions (i = 1, 2, 3).

$$D\vec{e}_i = \lambda_i \vec{e}_i \tag{4}$$

$$| D - \lambda I | = 0 \tag{5}$$

The calculated eigenvectors are ordered descending, and an ordered orthogonal basis with the first eigenvector having the direction of largest variance of the data is created (Goksel & Ozkan, 2006). In our sample, this leads to the principal diffusivity, and so the most appropriate diffusivity directions can be determined (Borisenko & Tarapov, 1979). The first principal component λ_1 has maximum variance, and thus its weighting coefficients give the direction of the maximum diffusion weighted signal, or largest principal diffusivity (Basser et al., 2000). The weighting coefficients of the second and third principal components λ_2 and λ_3 give the directions of the intermediate and smallest principal diffusivity respectively.
Estimating the fiber tract maps follow the implementation of the selected post processing methods, in this study the Hebbian learning rule, to resolve the related eigensystem. To begin the tracking process, generally a starting pixel also called a seed point is selected to focus on the desired region of interest and to avoid calculation overload in consideration of working on the whole brain DTMR data. Starting at the seed point coordinates, similar fiber orientation vectors are traced out upon a predefined similarity constraint until the selected ROI is fully covered. Specific tracts related to the investigated ROIs can be visualized by choosing the regions/seed points according to anatomical structures picked on the brain atlas where the selection can be made either on segmented DT brain map or unsegmented and full brain volume.

3. Hebbian learning for pattern association

3.1 Hebb's hypothesis

Hebb's rule is the earliest and the simplest of the learning rules for a neural network. The basic neural net model provides knowledge about the synaptic modifications and learning procedure between nodes in a pattern. The technique relies in representing the activity between correlated nodes according to their related weighting. The Organization of Behavior is expressed by Donald Hebb (1949) as: ``When the axon of cell A is near enough to excite a cell B and repeatedly or persistently takes part in firing it, some growth process or metabolic change takes place in one or both cells such that A's efficiency, as one of the cells firing B, is increased''. This Hebbian learning rule is used to store patterns in artificial neural network models of associative memory. The Hebb's postulate of learning implies both temporal and spatial constraints on learning.
The ability of the Hebb's rule to determine the weights for the correct output related to all the training pattern is influenced by three factors. One is the existence of such weights. Linear independency is a must to provide the existence of the weights. The second factor is the correlation factor. The quality of the resulting weight matrix of the Hebbian learning depends on the orthogonality of the input vectors. Finally, the weights of the Hebb's process represent the simultaneous activation of the stimulated nodes unit by unit, which lead the rule make also called correlation training or encoding (Fausett, 1994). The rule is sometimes called the activity product rule also, because of the correlational characteristic of Hebb's hypothesis.
The idea selecting the Hebbian learning to resolve the uncertainty problem in diffusion tensor tractography (DTT) relies in the proficiency of the neural networks as classifiers especially in non-linear real world problems. The Hebbian learning algorithm is performed locally, which makes the application a plausible theory for biological learning methods. That is also making Hebbian learning process ideal in DTT.

In this study, the input pattern is actually the eigensystem defining the principal diffusivity of the fibers in DTMRI. As previously mentioned, the learning theory of Hebb relies in the increase of the weights between neighboring nodes by simultaneous activation. In other words, the weights between the nodes of the input pattern in Hebbian learning are representing the relationship between these nodes. The modification of the weights and the implementation will be explained in the next subtitles.

3.2 Mathematical model of Hebb's rule

The formulation of the Hebbian learning follows with a synaptic weight w_{kj} of neuron k with F a function of both input signal x_j and output signal y_k (Haykin, 1999):

$$\Delta w_{kj}(n) = F(y_k(n), x_j(n)) \tag{6}$$

The Hebb's formula has many forms, the simplest form expressed with the weight modification is given as (Haykin, 1999):

$$\Delta w_{kj}(n) = \eta \; y_k(n) x_j(n) \tag{7}$$

The synaptic adjustment Δw_{kj} is applied to the synaptic weight vector w_{kj} at time step n with a learning rate parameter η. This proceeds from one step in the learning algorithm to another.

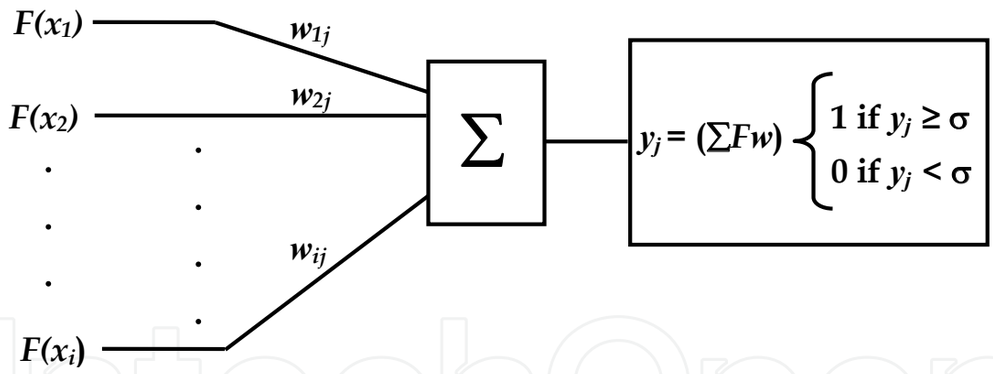

Fig. 1. The principal of the Hebbian learning: The activation function with a threshold σ is defining the output in other words activated, allowed vectors of the examined pattern

Generally, modification of a weight w_{ij} from an excited neuron x_i to a destination neuron y_j having a learning rate η, the Hebb's learning rule is defined formally as in Eq.(7) and expressed graphically as in Fig.1. Correlated nodes will have strong negative or positive weights regarding to their tendency being opposite or not, where uncorrelated nodes will have weights near zero. As a result, a neuron map is obtained with weights encoding the stationary probability density function of the input pattern vectors (Haykin, 1999). The procedure is an instance of unsupervised and competitive learning process. The advantages of the procedure is that it is a local learning rule, simple with very little computational requirement and biological plausibility.

As a basis of the proposed Hebbian method, independent component analysis (ICA) is applied to solve the intersecting fiber problem in DTT literature (Arfanakis et al., 2002; Sungheon et al., 2005; Jeong-Won & Singh, 2006). The application has provided useful information about the diffusion properties of brain structures without estimation of the diffusion tensor. But ICA should not be considered as a fiber tracking method. The technique maps structures. The advantage is that it may be used for visualization of particular structures without any user specific a priori information. Relying on the successful implementation of the ICA method in the literature, the basic Hebbian learning is proposed for the post processing of the diffusion weighted MR images.

3.3 The Hebbian rule in DTI

The fiber directions in living tissue should be compared carefully, thus simulation studies are done addressing verification and validation of the analysis. By generating the algorithm, first all the weights w_i=0 (i=1,…,n) are initialized. For each input training vector, the input units and the output unit are activated, while new weights are adjusted regarding Eq.(7). The weight modification Δw_{kj} follows until the ROI is covered according to the predefined constraints.

Our approach relies in the assumption that the axon follows a unique path. Each element in the Hebbian input pattern represents a voxel in the ROI, and each voxel is related with its neighboring voxels. To clarify the idea and the implementation steps, a sample synthetic fiber tract ROI with its eigenvectors in every pixel is given in Fig.2:

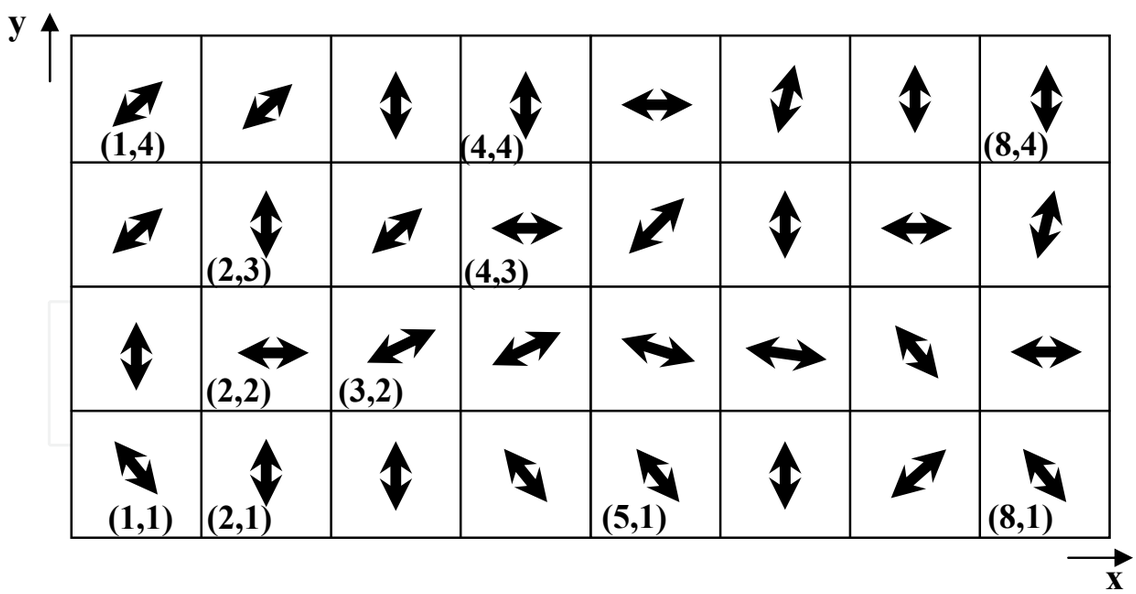

Fig. 2. A segment of synthetic fiber tract pattern illustrating the diffusion tensor orientations in each pixel with computed eigenvectors.

The seed point in Fig.2 is the voxel with the coordinate (4,2). The 8 neighboring nodes of the starting point are first investigated and in each step the weight is been updated. For the

same sample, Gaussian noise is added to the pattern, and again weights are updated starting from the same seed point. As a result, the Hebb rule defines the green path as the winning path (Fig.3). Depending on the threshold function varying branches can be determined for the same ROI (Fig.4). For simulation studies various threshold functions are selected to verify the algorithm, and to define the simulated paths more precisely. In living tissue, the selection of the threshold constraint is depending actually on the human brain atlas and anatomical structure knowledge.

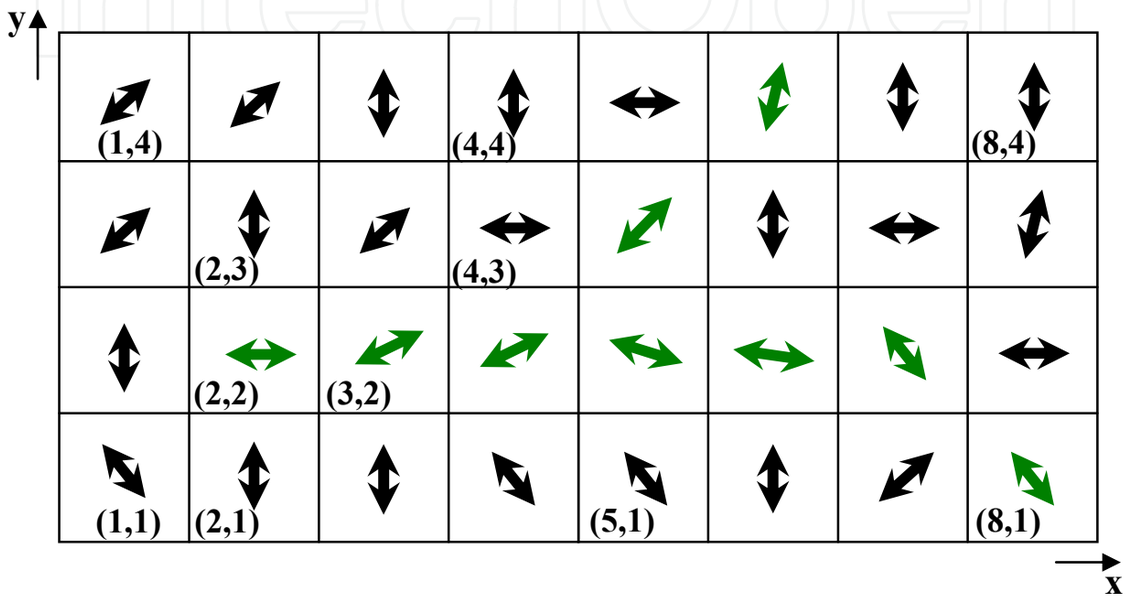

Fig. 3. The green branching path represents the winning tracts estimated by Hebb's learning

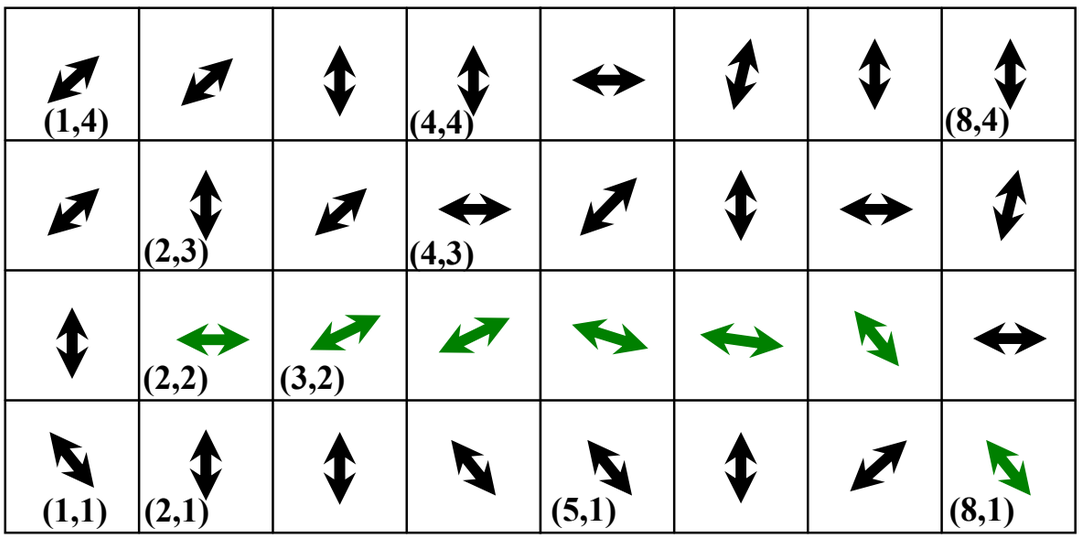

Fig. 4. For the same ROI, changing the threshold function results a non-branching trajectory

The real data sets of brain diffusion MR images are used for the validation of the algorithm. The starting point and the activation function's threshold are selected upon the knowledge of white matter fiber atlas and the most common pathology regions in the literature.

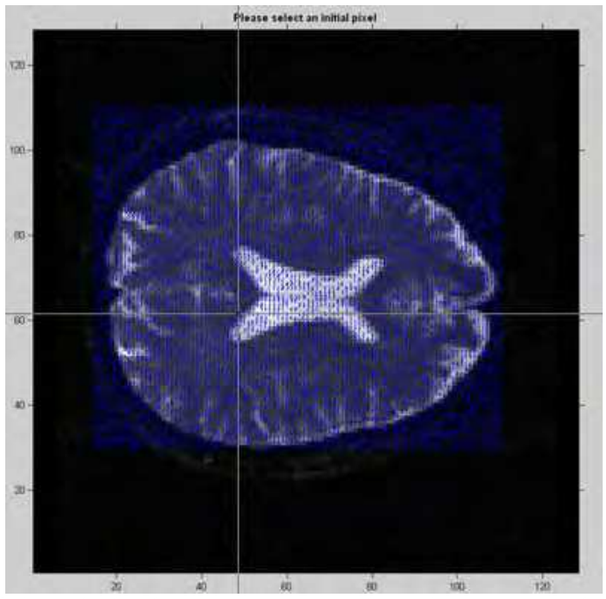

Fig. 5. Eigenvectors of the whole slice is represented on the registered anatomic MR image. The manually executed seed point selection is seen on the figure.

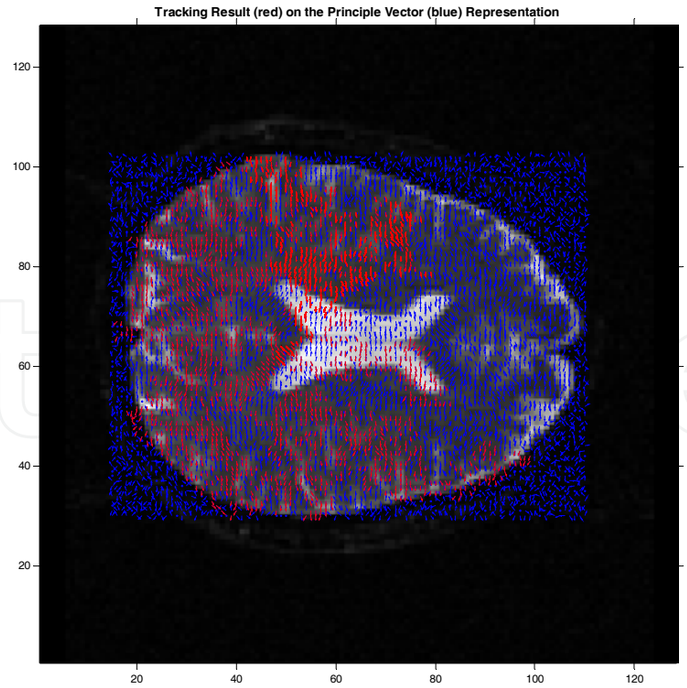

Fig. 6. Implementation of the algorithm at the starting point shown in Fig. 5 with a threshold function σ_1 allowing a wide range of neighbors as winning nodes results the represented axial slice registered with the anatomic MR image

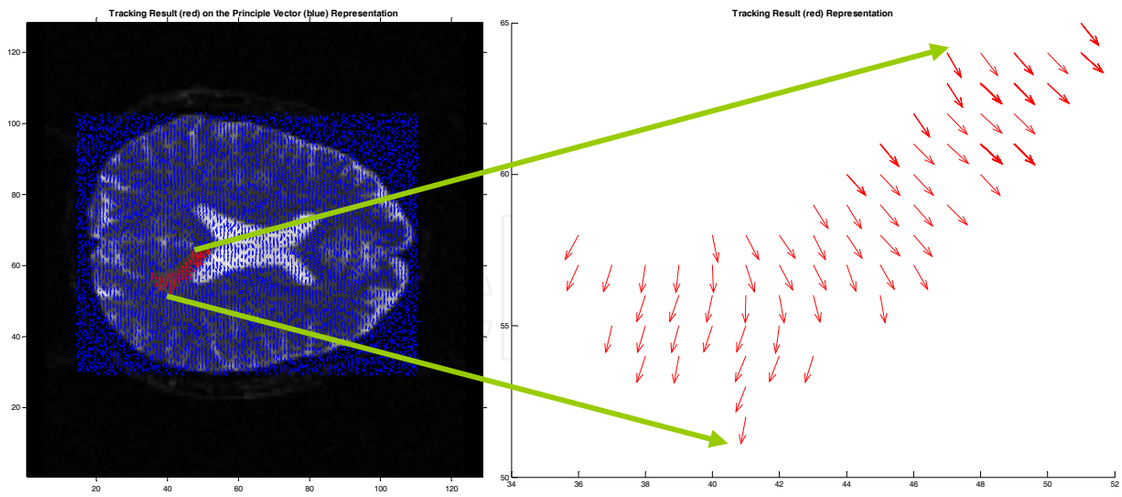

Fig. 7. Implementation of the algorithm with an activation function having a threshold σ_2 allowing a limited number of neighbors of the seed point shown in Fig. 5 as winning nodes

4. Discussion

The special class of artificial neural networks namely Hebbian learning is proposed for the analysis of a relatively new 3D imaging technique DTMRI's raw data. One of the major problems in DTI literature is the absence of a gold standard in fiber tractography. Intersections of two or more fiber tracts yield to erroneous estimates of the diffusivity and the fiber orientation. The anatomical fiber maps determined by diffusion tensor analysis are having still an unclear accuracy because of the inefficiency of the tensor model used to define the uncertainty regions such as crossing diffusivities in a single voxel. The practical accuracy of DT analysis and tractography vary upon the limitations of data quality and signal-to-noise ratio (SNR) (Mangin et al., 2002). In this proposed study the critical uncertainty problem is tried to be eliminated by adequate analysis tool. The method is first implemented on synthetic tract pattern (Fig. 2). The weight modifications yield to determine the weighted connections between the neighboring pixels (Fig. 3). The application results give promising tract estimations (Fig. 4) based on the threshold determination of the activation functions. Some real data analyses are done as represented in the implementation section 3.3 in Fig. 6 and Fig. 7. Still the proposed rule has to be implemented on 3D brain volume for validation studies.

Post processing reconstruction can reduce the sensitivity of tractography, so in Hebb application automated mapping and tracking after seed point selection is achieved and the method relies in basic learning algorithm which is quite an accepted procedure in defining the anatomical brain mapping. The applicability of the Hebbian rule to the uncertainty problem is verified by examining the updated weight changes by defining a fiber path.

The assumptions made in the determination of the diffusion tensor analysis are of great importance because the error tolerance and the general limitations of all the sequent applications including tractography are highly dependent on these.

5. Conclusion

Diffusion tensor imaging analysis and related tractography is highly promising for the detection and identification of brain fiber tracts especially the white matter paths. The implementation is helpful for better understanding of anatomical and pathological brain maps, the neural connectivity, neuropsychiatric diseases and the neural circuitry. The diffusion anisotropy in biological tissues still needs clarification on the fundamentals of its mechanisms. DTI is able to locate the intersecting fiber tracts but poor in identifying them, therefore post processing methods are of great importance (Lee, 2005; LeBihan, 2006). To solve the determination and visualization problems of fiber tracking especially in uncertainty regions, methods should be developed. The applied algorithm based on Hebbian learning is proposed to eliminate this uncertainty in intersecting pixels, and to define the fiber paths more secure and precisely upon the updated weightings.

The choice of training patterns plays a significant role in implementing the Hebb rule. The Hebbian approach aims basically the elimination of the impairment of the tensor modeling and the correlation of the brain fiber mapping to artificial neural network. The proposed method shows promising results to modify the fiber tractography and estimate the voxel diffusivity and neural map. The study must be accomplished in 3D human DTT. The assumptions made during the analysis need to be updated with a radiologist not to miss the clinical needs and to eliminate erroneous pathological approaches. Also engineering and clinical views should be obtained on the tractography results and these should be verified with brain atlases. The currently promising Hebb's rule will then be a qualified tool in DTMR analysis. Besides post processing enhancements, improvements will also be made with the development of faster sequences and higher field imaging.

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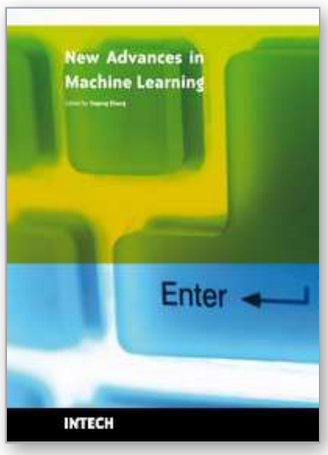

New Advances in Machine Learning

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The purpose of this book is to provide an up-to-date and systematical introduction to the principles and algorithms of machine learning. The definition of learning is broad enough to include most tasks that we commonly call “learning” tasks, as we use the word in daily life. It is also broad enough to encompass computers that improve from experience in quite straightforward ways. The book will be of interest to industrial engineers and scientists as well as academics who wish to pursue machine learning. The book is intended for both graduate and postgraduate students in fields such as computer science, cybernetics, system sciences, engineering, statistics, and social sciences, and as a reference for software professionals and practitioners. The wide scope of the book provides a good introduction to many approaches of machine learning, and it is also the source of useful bibliographical information.

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